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EXAMINER	
WHITEMAN, BRIAN A	
ART UNIT	**PAPER NUMBER**
1635	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/052,498	PATIERNO ET AL.	
	Examiner	Art Unit	
	Brian Whiteman	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 February 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *74-202* is/are pending in the application.

4a) Of the above claim(s) *153-202* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *74-152* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *4/11/02* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *7/3/02*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Non-Final Rejection

Claims 74-202 are pending.

Election/Restrictions

Applicant's election of Group I (claims 74-152) and species surgical intervention in the reply filed on 2/22/05 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 153-202 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention and radiation therapy, hormonal therapy, immunotherapy, chemotherapy, cryotherapy, and gene therapy in Claims 84, 96, 106, 117, 127, 134, and 144 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 2/22/05.

Upon a search of the prior art, the only prior art is under obviousness type double patenting. Thus, the non-elected species in claims 84, 96, 106, 117, 127, 134, and 144 are rejoined with the elected species (surgical intervention) and will be examined with the elected species.

Priority

The specification is objected to because the status of US 08/987,502 and US 09/556,467 needs updated because '502 and '467 are now US Patents.

Specification

Applicant is reminded of the proper language and format for an abstract of the disclosure.

The abstract should be in narrative form and generally limited to a single paragraph on a separate sheet within the range of 50 to 150 words. It is important that the abstract not exceed 150 words in length since the space provided for the abstract on the computer tape used by the printer is limited. The form and legal phraseology often used in patent claims, such as "means" and "said," should be avoided. The abstract should describe the disclosure sufficiently to assist readers in deciding whether there is a need for consulting the full patent text for details.

The language should be clear and concise and should not repeat information given in the title. It should avoid using phrases which can be implied, such as, "The disclosure concerns," "The disclosure defined by this invention," "The disclosure describes," etc.

The abstract of the disclosure is objected to because the abstract is longer than 15 lines. Correction is required. See MPEP § 608.01(b).

Claim Objections

Claims 74, 85, 97, 107, 118, 128, 135, and 145 are objected to because of the following informalities: the phrase "a uteroglobin" is grammatically incorrect. Appropriate correction is required.

Claims 81, 93, 103, 114, 124, 141, and 151 are objected to because of the following informalities: the term "gastrointestinal track" is misspelled. Suggest replacing the term with – gastrointestinal tract --. Appropriate correction is required.

Applicant is advised that should claim 74 be found allowable, claim 80 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Applicant is advised that should claim 85 be found allowable, claim 92 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Applicant is advised that should claim 97 be found allowable, claim 102 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Applicant is advised that should claim 107 be found allowable, claim 112 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing,

despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Applicant is advised that should claim 118 be found allowable, claim 123 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 74-152 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for 1) A method of inhibiting the growth of tumor cells of epithelial origin in a mammal, comprising direct administration of a vector comprising an uteroglobin gene and 2) The method of 1, further comprising another treatment selected from surgical intervention, radiation therapy, hormonal therapy, immunotherapy, chemotherapy, cryotherapy, and does not reasonably provide enablement for using a genus of administration routes to treat a tumor in vivo using the vector. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

> Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized in In re Wands, 858 F.2d 731, 8USPQ2d 1400 (Fed. Cir. 1988). They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence

or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

The claimed invention is a method of treating a tumor (tumor of epithelial origin) in a mammal comprising in vivo administration of a polynucleotide sequence encoding uteroglobin. In addition, the claimed invention encompasses the method described above further comprising treating the tumor with another treatment, wherein the other treatment is surgical intervention, radiation therapy, hormonal therapy, immunotherapy, chemotherapy, cryotherapy, and gene therapy. The invention lies in the field of cancer gene therapy.

At the time the application was filed, gene therapy was considered to be unpredictable due to significant problems in several areas. The state of the art as exemplified Anderson et al (EK), displays major consideration for any gene transfer or any DNA therapy protocol involve issues that include:

1) The type of vector and amount of DNA constructs to be administered,

2) The route and time course of administration, the sites of administration, and successful uptake of the claimed DNA at the target site;

3) The trafficking of the genetic material within cellular organelles, the rate of degradation of the DNA, the level of mRNA produced, the stability of the mRNA product, the amount and stability of the protein produced, and

4) What amount of the expressed proteins considered to be therapeutically effective for a DNA therapy method.

In addition, all of these issues differ dramatically based on the specific vector used, the route of administration, the animal being treated, therapeutically effective amount of the DNA, and the disease being treated.

Anderson teaches that gene therapy is a powerful new technology that still requires several years before it will make a noticeable impact on the treatment of disease, and that several major deficiencies still exist including poor delivery systems, both viral and non-viral, and poor gene expression after genes are delivered (pp. 25-30).

Anderson further teaches that the reason for the low efficiency of gene transfer and expression in human patients is that we still lack the basis understanding of how vectors should be constructed what regulatory sequences are appropriated for which cell types (page 30, column 1, last paragraph). Furthermore, Verma, (FJ), indicates that factors including the nature of the diseases and/or disorders, the nature of a DNA and/or target tissue, and a delivery system and/or amounts of the DNA complexes employed in the delivery system that would generate a therapeutic effect *in vivo* must be considered for any gene therapy method to be successful (page 238, columns 1 and 2). For additional views of the unpredictability of the gene therapy art (cancer gene therapy), see Gomez-Navarro et al. (FD) and Vile (GA). Thus, at the time the application was filed, the state of the art of gene therapy is considered highly unpredictable.

The applicants describes several in vitro experiments showing 1) Uteroglobin inhibits invasiveness of tumor cells derived from human prostate cancer and art of epithelial cell origin, DU-145, LNCaP, PC3-M, and TSU-Prl (examples 3-9). 2) Uteroglobin inhibits arachidonic acid release by fibroblast conditioned media (FCM) stimulated DU-145 cells. 3) Uteroglobin was not expressed in a male's prostatic adenocarcinoma cells (example 19). 4) Uteroglobin mRNA is not

detected or is aberrantly processed in cells derived from metastases of human prostatic tumors (Example 20). Furthermore, the applicants contemplate DNA therapy using uteroglobin in patients with metastatic adenocarcinoma, or tumor of the breast, epithelial origin (examples 11-18). In example 21, the applicants contemplate performing therapy on a patient with prostate cancer. In addition, the applicants contemplate using a method of gene therapy comprising an adenovirus-based plasmid expression vector containing the uteroglobin gene linked to the promoter of the PSA gene after a patient undergoes radical prostatectomy (example 22).

In view of the teachings in the instant specification and the prior art, the applicants provide sufficient guidance and/or factual evidence to practice the claimed methods using direct administration. However, the applicants do not provide sufficient guidance for how the in vitro experiments described in the instant specification reasonably correlate to an in vivo method of gene therapy for treating tumors using a polynucleotide, which encodes uteroglobin using a genus of administration routes. The claimed methods embrace a genus of administration routes and the applicants do not provide sufficient guidance and/or factual evidence for how all routes of administration would provide a therapeutic response when treating an in vivo tumor. The state of the art at the time the application was filed for the route of administration for gene therapy as exemplified by Vile (supra) and Verma (supra) indicates that factors including the nature of the diseases and/or disorders, the nature of a DNA and/or target tissue, and a delivery system and/or amounts of the DNA complexes employed in the delivery system that would generate a therapeutic effect *in vivo* must be considered for any gene therapy method to be successful (page 238, columns 1 and 2). In view of the art of record, it is not apparent to one skilled in the art how to reasonably extrapolate from the in vitro results taught in the instant

specification to a genus of administration routes besides direct administration to generate a therapeutic response in an in vivo tumor. Therefore, it would take one skilled in the art an undue amount of experimentation to determine what route of administration (*e.g.* intravenous, intramuscular, non-invasiveness, or topical administration) other than direct administration to the tumor in a mammal would result in a therapeutic response using a polynucleotide encoding uteroglobin.

In addition, with respect to inhibiting tumorigenesis of a tumor of epithelial origin set forth in instant claims 74-84, the broadest claims read on a method of inhibiting a tumor of epithelial origin already present in a subject from growing or preventing a tumor of epithelial origin that is not present in a subject from growing. Thus, the claims are considered broad. The applicants teach inhibiting tumors already present from further growing (pages 98-99). However, the relevance of this data to preventing a tumor in vivo is unclear at best because neither the applicants nor the prior art provide a correlation or nexus between the results obtained in the studies such as those provided by applicants with results which the skilled artisan would reasonably expect to see in vivo for preventing a tumor. The applicants do not teach preventing tumors of epithelial origin in a subject. The art of record is absent for preventing a tumor in a subject. Thus, to the extent the claims fail to recite distinguishing features to commensurate with the level of guidance presented, the claims are not considered enabled.

In addition, with respect to claims 118-127 and 135-152, the broadest claims read on treating all tumors comprising in vivo administration of a vector, to a mammal, a polynucleotide encoding an uteroglobin. Thus, the claims are considered broad. The applicants teach treating tumor cells of epithelial origin using the claimed method. However, the relevance of this data to

treating a genus of tumors in vivo is unclear at best because neither the applicants nor the prior art provide a correlation or nexus between the results obtained in the studies such as those provided by applicants with results which the skilled artisan would reasonably expect to see in vivo for treating a genus of tumors in vivo. The applicants do not teach treating tumors of non-epithelial origin (e.g., brain tumor). The art of record teaches that one skilled in the art can not reasonably extrapolate from treating one type of cancer (cancer of epithelial origin) to treating another type of cancer (cancer of non-epithelial origin) without an undue amount of experimentation and the art of record teaches that there is no universal protocol that can be reasonably extrapolated from one type of cancer gene therapy to a genus of gene therapy methods. See Gomez-Navarro (supra) and Vile (supra).

In addition, with respect to claims 145-152, the claims are directed to repairing a dysfunctional gene to prevent or inhibit metastasis of a cancer, comprising in vivo administration in a vector, to a mammal, of a polynucleotide sequence, which encodes an uteroglobin. The claimed method reads on repairing a genus of dysfunctional genes (e.g., dystrophin, spectrin, p53, pRb, Factor VIII, etc.) to treat a tumor of epithelial origin (e.g., prevent or inhibi1t metastasis of the tumor, inhibiting tumorigenesis of a tumor of epithelial origin). The claims must be considered broad. The applicants teach that in situ hybridization analysis of a tumor biopsy reveals that the uteroglobin gene is not being expressed in tumor cells (page 95). The specification does not disclose using the claimed method to repair a genus of dysfunctional genes. The closest prior art teaches a method of preventing metastasis in a tumor using uteroglobin. See US 6,316,416. The specification only provides sufficient guidance and/or factual evidence for repairing a dysfunctional uteroglobin gene by administering a

polynucleotide encoding uteroglobin directly to the tumor in vivo. Thus, to the extent the claims fail to recite distinguishing features to commensurate with the level of guidance presented, the claims are not considered enabled.

In addition, the claimed invention contemplates treating a mammal with cancer using a viral composition encoding an uteroglobin polynucleotide or fragment thereof, and further comprising another treatment. See instant claims 84, 96, 106, 117, 127, 134, and 144. The prior art teaches a method of treating cancer in a patient using uteroglobin in combination with other treatments. See US 6,316,416. The art of record provides sufficient guidance for using a combination method comprising a genus of other treatments, including surgical intervention, immunotherapy, radiation therapy, hormonal therapy, immunotherapy, chemotherapy, and cryotherapy. The combination comprising the claimed method in combination with a genus of gene therapy methods is not considered enabled. The applicants contemplate using ex vivo gene therapy or administering polynucleotides that encode anti-metastatic agents, preferably inhibitors of arachidonic acid release (uteroglobin and lipocortins). See pages 72-77 of the instant specification. However, the applicants do not provide sufficient guidance for how all methods of gene therapy would display an enhanced therapeutic effect in combination with a polynucleotide encoding an uteroglobin. In view of the art of record and the instant specification, it would require one skilled in the art an undue amount of experimentation to determine how to obtain an enhanced therapeutic response for treating a subject with a tumor using the claimed composition and an another treatment, wherein the other treatment is a genus nucleic acid encoding therapeutic polypeptide (Factor, VIII, Factor IX, dystrophin, insulin, etc.). Thus, it not apparent to one skilled in the art what polynucleotide encoding a therapeutic polypeptide other than

uteroglobins and lipocortins would display a therapeutically enhanced effect in combination with the polynucleotide encoding an uteroglobin.

In conclusion, the as-filed specification and claims coupled with the art of record at the time the invention was made provide enablement for 1) A method of inhibiting the growth of tumor cells of epithelial origin in a mammal, comprising direct administration of a vector comprising an uteroglobin gene and 2) The method of 1, further comprising another treatment selected from surgical intervention, radiation therapy, hormonal therapy, immunotherapy, chemotherapy, and cryotherapy, but not for the breadth of the claimed embodiment. Given that gene therapy wherein a polynucleotide was employed to correct a disease or a medical condition in a mammal was unpredictable at the time the application was filed, and given the lack of sufficient guidance as to a gene therapy method for treating an in vivo tumor using a genus of administration routes, one skilled in the art would have to engage in a large quantity of experimentation in order to practice the claimed invention based on the applicant's disclosure and the unpredictability of gene therapy.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 74-84 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1 and 2 of U.S. Patent No. 6,395,715. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims and the claims from '715 are directed to using a vector encoding a uteroglobin gene to treat tumor cells of epithelial origin in a mammal and further comprising additional treatment selected from surgical intervention, radiation therapy, hormonal therapy, immunotherapy, chemotherapy, and cryotherapy.

The claims from '715 do not specifically recite using a polynucleotide sequence selected from the group consisting of RNA, a DNA, a DNA cloned in to a DNA vector, and a DNA cloned in a DNA vector encapsidated in a viral capsid. In addition, the claims from '715 do not specifically recite using human uteroglobin. In addition, the claims from '715 do not specifically recite the limitation in instant claim 81 and 82. However, when reading the definition for the term polynucleotide in the specification of '715, the limitations of using a polynucleotide set forth in instant claim 76, 77, and 78 would be an obvious variant of the instant claims because the specification defines a polynucleotide as a polynucleotide selected from RNA, DNA, DNA vector, viral vector comprising the DNA as the polynucleotide in the method. See column 26. See MPEP 804, which recites: The specification can always be used as a dictionary to learn the meaning of a term in the patent claim. In re Boylan, 392 F.2d 1017, 157 USPQ 370 (CCPA 1968). In addition, when reading the definition of the term uteroglobin in the specification of '715, it would have been obvious to one of ordinary skill in the art to use human uteroglobin in

the method because the specification defines human uteroglobin as an uteroglobin. See columns 17-18. In addition, when reading the definition in the specification of '715, it would be obvious to one of ordinary skill in the art to treat a tumor of epithelial origin using the method because the specification defines what type of tumors of epithelial cell origin is embraced by the claimed method. See column 22. Therefore, the claims of the instant application and US patent '715 are obvious variants of one another.

Claims 85-152 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1 and 2 of U.S. Patent No. 6,395,715 in view of US 6,316,416. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims and the claims from '715 are directed to using a vector encoding a uteroglobin gene to treat tumor cells of epithelial origin in a mammal and further comprising additional treatment selected from surgical intervention, radiation therapy, hormonal therapy, immunotherapy, chemotherapy, and cryotherapy.

The claims from '715 do not specifically recite the preamble of instant claims 85-87, 97, 107, 118, 128, 135, and 145.

However, at the time the invention was made, the claims from '416 teach that uteroglobin delivered to tumor cells results in the preamble set forth in instant claims 85-87, 97, 107, 118, 128, 135, and 145. The claims from '416 do not specifically recite how the uteroglobin is administered to the patient. However, the pre-amble in the instant claims would be obvious variants of the claimed method in '715 taken with the claims from '416 because one of ordinary skill in the art would reasonably determine that by expressing uteroglobin in a tumor via a

method of gene transfer as recited in '715, the expression of uteroglobin would result in the mechanism(s) recited in the preamble of the instant claims.

The claims from '715 do not specifically recite the limitation of instant claims 89-91, 99-101, 109-111, 120-122, 130-132, 137-139, and 147-149. However, when reading the definition in the specification of '715, the limitations of using a polynucleotide set forth in instant claim 76, 77, and 78 would be an obvious variant of the instant claims because the specification teaches using a polynucleotide selected from RNA, DNA, DNA vector, viral vector comprising the DNA as the polynucleotide in the method. See column 25. See MPEP 804.

The claims from '715 do not specifically recite using the limitation in instant claims 88, 98, 108, 119, 129, 136, 146. However, when reading the definition in the specification of '715, it would have been obvious to one of ordinary skill in the art to use human uteroglobin in the claimed method because the specification teaches human uteroglobin as the uteroglobin. See Columns 17-18.

The claims from '715 do not specifically recite the limitation of instant claims 93, 94, 103, 104, 113, 114, 115, 124, 125, 141, 142, 151, and 152. However, when reading the definition in the specification of '715 in view of the claims of '715, it would be obvious to one of ordinary skill in the art to treat a tumor of epithelial origin using the method because the specification defines what type of tumor of epithelial cell origin is embraced by the claimed method. See Column 22.

Therefore, the claims of the instant application and US patent '715 taken with US patent '416 are obvious variants of one another.

Claims 74-152 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-89 of U.S. Patent No. 6,316,416. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims and the claims from '416 are directed to administering uteroglobin to treat a tumor of epithelial origin in a patient and further comprising additional treatment selected from surgical intervention, radiation therapy, hormonal therapy, immunotherapy, chemotherapy, and cryotherapy.

The claims from '416 do not specifically recite using a polynucleotide encoding uteroglobin in the methods. However, the claims do not specifically define how the uteroglobin is delivered to the patient (There is no election/restriction of record between polypeptide and DNA therapy in the prosecution history of '416). However, the claims are considered broad for how the uteroglobin is delivered to the tumor and the specification of '416 teaches using polynucleotide to delivery the uteroglobin to the tumor (columns 24-26 and 37). Thus, one of ordinary skill in the art would have been motivated to use a polynucleotide encoding uteroglobin in a method of treating a tumor of epithelial origin in vivo comprising direct administration of the vector to the tumor because delivering uteroglobin to a tumor in vivo was disclosed by the specification of '416. Therefore, the claims of the instant application and US patent '416 are obvious variants of one another.

Claims 74-81, 83-93, 95-103, 105-112, 114, 116-124, 126-127, 135-141, and 143-151 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-9 of U.S. Patent No. 6,509,316. Although the conflicting claims are

not identical, they are not patentably distinct from each other because the instant claims and the claims from '316 are directed to delivering uteroglobin to a tumor of epithelial origin. The instant claims are directed to delivering a polynucleotide encoding uteroglobin and the claims from '316 are directed to delivering human uteroglobin. However, the claims from '316 are broad and encompass delivering human uteroglobin using any method disclosed in the specification of '316 (e.g., polynucleotide delivering to the tumor). See columns 24-26. The claims from '316 do not recite the mechanism used for treating a tumor in the preamble of instant claims 74, 85, 97, 107, 118, 135, and 145. However, the preambles of the instant claims would be obvious variants of treating a lung cancer using uteroglobin because delivering a polynucleotide encoding uteroglobin to the cancer would result when practicing the claimed method in '316. Note: there is no election/restriction between polynucleotide and polypeptide therapy in the prosecution history of '316. Therefore, the claims of the instant application and US patent '316 are obvious variants of one another.

Claims 74-152 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-7 of U.S. Patent No. 6,358,915. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims and the claims from '915 are directed to delivering uteroglobin to a tumor of epithelial origin. The instant claims are directed to delivering a polynucleotide encoding uteroglobin and the claims from '915 are directed to delivering uteroglobin. However, the claims from '915 are broad and encompass delivering uteroglobin using any method disclosed in the specification of '915 (e.g., polynucleotide delivering to the tumor). See columns 23-24 and

36. In addition, claim 7 of '915 contemplates using gene therapy in the claimed method recited in claim 1 of '915. The claims from '915 do not specifically recite the mechanism used for treating a tumor in the preamble of instant claims 74, 85, 97, 107, 118, and 145. However, the preambles of the instant claims would be obvious variants of treating a cancer of epithelial origin using uteroglobin because delivering a polynucleotide encoding uteroglobin to the cancer would result when practicing the claimed method in '915. Note: there is no election/restriction between polynucleotide and polypeptide therapy in the prosecution history of '915. Therefore, the claims of the instant application and US patent '915 are obvious variants of one another.

Claims 74-152 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-7, 12-17, 22-27, 32-34, and 38-43 of U.S. Patent No. 6,335,321. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims and the claims from '321 are directed to delivering uteroglobin to a tumor of epithelial origin. The instant claims are directed to delivering a polynucleotide encoding uteroglobin and the claims from '321 are directed to delivering uteroglobin. However, the claims from '321 are broad and encompass delivering uteroglobin using any method disclosed in the specification of '321 (e.g., polynucleotide delivering to the tumor). See columns 24-26 and 36. In addition, claims 7, 17, 27, and 34 of '321 contemplate using gene therapy in the claimed method. The claims from '321 do not specifically recite the mechanism used for treating a tumor in the preamble of instant claims 97, 118, and 145. However, the preambles of the instant claims would be obvious variants of treating a cancer of epithelial origin using uteroglobin because delivering a polynucleotide

encoding uteroglobin to the tumor would result when practicing the claimed method in '321. Note: there is no election/restriction between polynucleotide and polypeptide therapy in the prosecution history of '321. Therefore, the claims of the instant application and US patent '321 are obvious variants of one another.

Claims 74-152 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-4, 9-12, and 17-20 of U.S. Patent No. 6,288,039. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims and the claims from '039 are directed to delivering uteroglobin to a tumor of epithelial origin. The instant claims are directed to delivering a polynucleotide encoding uteroglobin and the claims from '039 are directed to delivering uteroglobin. However, the claims from '039 are broad and encompass delivering uteroglobin using any method disclosed in the specification of '039 (e.g., polynucleotide delivering to the tumor). See columns 27-29 and 40-41. In addition, claims 3, 11, and 19 of '039 contemplate using gene therapy in the claimed method. The claims from '039 do not specifically recite the mechanism used for treating a tumor in the preamble of instant claims. However, the preambles of the instant claims would be obvious variants of treating a cancer of epithelial origin using uteroglobin because delivering a polynucleotide encoding uteroglobin to the tumor would result when practicing the claimed method in '039. Note: there is no election/restriction between polynucleotide and polypeptide therapy in the prosecution history of '039. Therefore, the claims of the instant application and US patent '039 are obvious variants of one another.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian Whiteman whose telephone number is (571) 272-0764. The examiner can normally be reached on Monday through Friday from 7:00 to 4:00 (Eastern Standard Time), with alternating Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang, acting SPE – Art Unit 1635, can be reached at (571) 272-0811.

Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center number is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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